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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/302,863	04/30/1999	RAYMOND G. GOODWIN	2519	7568

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EXAMINER

ROMEO, DAVID S

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 04/10/2002

18

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.

09/302,863

Applicant(s)

GOODWIN ET AL.

Examiner

David S Romeo

Art Unit

1647

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 25 February 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 25 February 2002. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will not be entered because:
- (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☒ they raise the issue of new matter (see Note below);
- (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: 15-34.

Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.
10. ☐ Other: _____

David S. Romeo
David S Romeo
Primary Examiner
Art Unit: 1647

Continuation of 2. NOTE: The proposed amendments to the specification raise the issue of new matter and require further consideration. The proposed amendments to the claims raise the issue of new matter and require further consideration because the proposed amendments to the specification incorporate a definition for "the extracellular domain" and the claims recite the limitation "the extracellular domain" and the proposed amendments to the specification raise the issue of new matter and require further consideration. The proposed amendments to the claims would require further consideration and/or search because they recite the limitation "the extracellular domain" and the limitation has not been previously considered and/or searched. The proposed amendments to the claims, i.e. the deletion of the terms "TACI" and "TACI-L", would have appeared to obviate the proposed amendments to the specification if the proposed claim amendments would have been entered. The proposed amendment does not comply with 37 CFR 1.121(b)(1)(iii). 37 CFR 1.121(b)(1)(iii) requires that a separate version of the replacement paragraph(s) accompany the amendment. The separate version must include each replacement paragraph with markings to show the changes relative to the previous version as an aid to the examiner. 37 CFR 1.121. The version with markings to show changes made in the specification provided with the proposed amendment does not have markings to show the changes made. The claim amendments would require further consideration of the antecedent basis for the terms "TACI" and "TACI-L".

Continuation of 5. does NOT place the application in condition for allowance because: Regarding the rejection of claims 15-34 under 35 U.S.C. 112, first paragraph, Applicants argue that undue experimentation is not required to practice the invention because screening assays involve well-established procedures, that any experimentation required is routine. Applicants arguments have been fully considered but they are not persuasive. Although screening assays involve well-established, routine procedures, if the material used to used to achieve such assays are not enabled then the such assays are not enabled. The present specification has not enabled polypeptides encoded by nucleic acid molecules at least 75% identical to SEQ ID NO: 1 or SEQ ID NO: 3.

Applicants argue that the specification describes proteins having at least 75% identity at page 6, lines 4-26 and page 7, lines 10-27, that the specification teaches how to calculate % identity, that the specification teaches Southern hybridizations, that all the polypeptides must retain biological activity permitting one skilled in the art to identify those embodiments encompassed by the claim, that assays are provided for testing binding. Applicants arguments have been fully considered but they are not persuasive. The claims are directed to or encompass polypeptides encoded by nucleic acid molecules at least 75% identical to SEQ ID NO: 1 or SEQ ID NO: 3. However, % identity at the nucleotide level translates into a much lower % identity at the amino acid level and the instant specification the instant specification does not identify those amino acid residues in the amino acid sequence of a TACI or a TACI-L which are essential for their biological activity and structural integrity and those residues which are either expendable or substitutable. Page 6, lines 4-26 and page 7, lines 10-27, of the present application do not identify those amino acid residues in the amino acid sequence of a TACI or a TACI-L which are essential for their biological activity and structural integrity and those residues which are either expendable or substitutable. In the absence of this information a practitioner would have to resort to a substantial amount of undue experimentation in the form of insertional, deletional and substitutional mutation analysis before they could even begin to rationally design a functional TACI or TACI-L having other than a natural amino acid sequence. Furthermore, there are no working examples of such variant polypeptides. Moreover, there is a lack of predictability in the art. Applicant has taken the position that 35 U.S.C. § 112, first paragraph, permits an artisan to present claims of essentially limitless breadth so long as the specification provides one with the ability to test any particular embodiment which is encompassed by the material limitations of a claim and thereby distinguish between those embodiments which meet the functional limitations from those that don't. This argument is not entirely without merit. However, the issue here is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance provide by the instant specification and the prior art of record. Applicant's 'make and test' position is inconsistent with the provisions 35 USC 112, first paragraph, because instant specification provides no working examples and no guidance that would permit an artisan to practice the invention commensurate with the scope of the instant claims. To practice the instant invention in a manner consistent with the breadth of the claims would not require just routine experimentation or a repetition of work that is described in the instant application, but a substantial inventive contribution on the part of a practitioner which would involve the determination of those amino acid residues in the amino acid sequence of TACI or a TACI-L which are required for their functional and structural integrity. It is this additional characterization that is required in order to obtain the functional and structural data needed to permit one to produce a polypeptide which meets both the structural and functional requirements of the instant claims that constitutes undue experimentation. The first paragraph of 35 U.S.C. § 112 requires that the breadth of the claims must be based upon the predictability of the claimed subject matter and not on some standard of trial and error. Unless one has a reasonable expectation that any one material embodiment of the claimed invention would be more likely than not to function in the manner disclosed or the instant specification provides sufficient guidance to permit one to identify those embodiments which are more likely to work than not without actually making and testing them then the instant application does not support the breadth of the claims.

Regarding the rejection of claim(s) 15-34 are rejected under 35 U.S.C. § 112, second paragraph, the proposed amendment would have overcome the rejection of the claims in which the terms "TACI" and "TACI-L" would have been deleted if the proposed amendment had been entered.

Regarding the rejection of claims 15, 19, 20, 23, 25, 29-34 under 35 U.S.C. 103(a) as being unpatentable over Chaudhary (6, cited by Applicants) in view of Bringman (a11) and further in view of Bram (13, cited by Applicants), Applicants argue that that prima facie case for obviousness has not been set forth. Applicants arguments have been fully considered but they are not persuasive. BJAB cells, a human B cell line, were treated with TNRL1-alpha and their survival was significantly reduced (Chaudhary at page 118, lines 4-16). It is further noted that Bram (13, cited by Applicants) teaches the amino acid sequence of a human transmembrane lymphocyte receptor (TACI) (Figure 2) that is normally present in all B-cells (paragraph bridging pages 3-4). The amino acid sequence of TACI is 100% identical to Applicants' SEQ ID NO: 2. It is further noted that BJAB is a human B cell line. BJAB cells comprise TACI, absent evidence to the contrary. Treating BJAB cells with TNRL1-alpha and assaying for cell survival, as taught by Chaudhary, is a method comprising forming a composition comprising a TACI protein and a TACI-L protein and assaying for the level of interaction of the TACI protein and the TACI-L protein, wherein the interaction of TACI and TACI-L is identified. Bringman does teach the desirability of raising neutralizing antibodies that inhibit receptor-ligand interactions. One of ordinary skill in the art would be motivated to make a neutralizing antibody, as taught by Bringman, against TNRL1-alpha and to test that antibody for neutralization of TNRL1-alpha bioactivity in the BJAB cell survival assay because such an antibody would facilitate characterization and purification of TNRL1-alpha. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on

obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper.

Regarding the objection under 35 U.S.C. 132 to the amendment filed 03/19/2001 (Paper No. 14) because it introduces new matter into the disclosure, Applicants argue that the amendatory material of March 19, 2002 has been canceled and that the specification has been amended to properly include the material incorporated by reference, that Applicants have submitted a declaration signed by Applicants' representative stating that the amendatory material consists of the same material incorporated by reference. Applicants arguments have been fully considered but they are not persuasive. The amendatory material is not supported by the original disclosure because the original disclosure merely contains a reference to the foreign patent document but the amendatory material consists of only a portion(s) of the foreign patent document, and, hence, does not consists of the same material incorporated by reference in the referencing application, and there is no basis in the original disclosure for incorporation of those specific proteins, and the application as filed does not direct particular attention to specific portions of the referenced document where the subject matter being incorporated may be found. It is further noted that deletion of all references to TACI and TACI-L in the claims would appear to obviate the necessity of amending the specification to define TACI and TACI-L, but the issue with respect to "the extracellular domain" (see above) would remain.

Regarding the rejection of claims 15, 29, 30 and claims 33, 34 under 35 U.S.C. 112, second paragraph, Applicants arguments are directed to the proposed amended claims and those amendments have not been entered.